COHN LIFLAND PEARLMAN
HERRMANN & KNOPF LLP
PETER S. PEARLMAN
Park 80 West – Plaza One
250 Pehle Avenue, Suite 401
Saddle Brook, NJ 07663
Telephone: 201/845-9600
201/845-9423 (fax)

Liaison Counsel

ROBBINS GELLER RUDMAN
& DOWD LLP
PATRICK J. COUGHLIN
ARTHUR C. LEAHY
SCOTT H. SAHAM
LUCAS F. OLTS
MATTHEW I. ALPERT
JENNIFER L. GMITRO
655 West Broadway, Suite 1900
San Diego, CA 92101
Telephone: 619/231-1058
619/231-7423 (fax)

Counsel for Plaintiffs

[Additional counsel appear on signature page.]

UNITED STATES DISTRICT COURT

DISTRICT OF NEW JERSEY

ALASKA ELECTRICAL PENSION FUND, et al., On Behalf of Themselves and All Others Similarly Situated, Plaintiffs, vs. PHARMACIA CORPORATION, et al., Defendants.	No. 03-1519 (AET) **(Consolidated)** CLASS ACTION PLAINTIFFS' SUPPLEMENTAL STATEMENT OF DISPUTED MATERIAL FACTS

CONFIDENTIAL – FILED UNDER SEAL

TABLE OF CONTENTS

Page

Page

Background to the CLASS Study

1. Before the period April 17, 2000 through August 5, 2011 (the "Class Period"), patients with osteoarthritis and rheumatoid arthritis were often treated with a class of medications called non-steroidal anti-inflammatory drugs ("NSAIDs") such as ibuprofen. Ex. 62 at 5.[1] Unfortunately, NSAIDs suffer from a very serious drawback: they often cause ulcers and ulcer complications. *Id.* Ulcer complications can include perforation (a hole in the stomach), obstruction (a blockage of the intestine), and bleeding. *Id*. During the Class Period, NSAID-associated ulcers and ulcer complications resulted as many as 20,000 per year in the U.S. alone. Ex. 63 at 2. Before the Class Period, all NSAID carried labels containing a warning that they may cause severe gastrointestinal ("GI") side effects (the "NSAID GI Warning"). Ex. 62 at 5.

2. Cox-2 inhibitors were developed to hopefully treat the pain and inflammation of arthritis as effectively as NSAIDs but without the GI side effects. Ex. 63 at 2. G.D. Searle & Co. ("Searle") developed celecoxib[2] as its entry in the emerging market for Cox-2 inhibitors.

---

[1] All exhibits referenced herein are attached to the Declaration of Scott H. Saham in Support of Plaintiffs' Opposition to Defendants' Motion for Summary Judgment, unless otherwise noted.

[2] Celecoxib was marketed under the trade name "Celebrex." Throughout this document, the terms "Celebrex" and "celecoxib" are equivalent.

3. Searle submitted the new drug application ("NDA") for Celebrex with the FDA on July 29, 1998. Ex. 59 (May 25, 2011 Expert Report of Debra Bowen, M.D., FACAAI ("Bowen Report")) at 11 n.13. Celebrex was approved for the treatment of osteoarthritis and rheumatoid arthritis on December 31, 1998. *Id.* at 13 n.24. At the time of its approval, the label for Celebrex contained the same NSAID GI warning as ibuprofen and other NSAIDs. *Id.* at 26 n.132.

4. Searle and Pfizer Inc. ("Pfizer") co-marketed Celebrex after initial FDA approval. Ex. 93. Even with the NSAID GI warning on its label, Celebrex was the most successful drug launch in history up to that point, with sales of over $1.4 billion in 1999. Ex. 109 at 337; Ex. 110 at 499. Nonetheless, Celebrex cost much more than older NSAIDs and it had never been proven safer or more effective. Ex. 63 at 2. In light of Celebrex's high cost and unproven benefits, certain HMOs limited access to Celebrex until long-term data proving its GI safety advantage became available. Ex. 106 at 503.

5. The FDA letter approving Celebrex stated "[w]e remind you of your Phase 4 commitment . . . . This commitment is to study the effects of Celebrex on using a protocol agreed to by the review Division." Ex. 111 at 002. Searle/Pharmacia Corporation ("Pharmacia") was thus obligated to conduct another trial of Celebrex as a condition of FDA approval. Ex. 107 (December 16, 2011 Deposition Transcript of Debra Bowen, M.D. ("Bowen Depo.")) at 190:10-21. That trial eventually came to be called the Celecoxib [Celebrex] Long-term Arthritis Safety Study, or CLASS.

6. The purpose of the CLASS study was to prove that Celebrex had better GI safety than NSAIDs in order to remove or significantly modify the NSAID GI Warning on Celebrex's label. Ex. 112 at 984-85; Ex. 2 (September 22, 2010 Deposition Transcript of Pfizer Vice President Ethan Weiner ("Weiner Depo.")) at 32:2-11; Ex. 17 (August 19, 2010 Deposition Transcript of Pfizer Global Candidate Team Leader Leland Loose, Ph.D. ("Loose Depo.")) at 75:5-11. Searle estimated that removal of the NSAID GI Warning would add another $300 million in Celebrex sales per year. Ex. 79 at 798.

7. Searle designed the study in collaboration with the FDA. Ex. 60. Searle met with the FDA several times between October 22, 1997 and September 22, 1998 regarding the design of the CLASS trial. Ex. 59 (Bowen Report) at 12. At these meetings, the FDA told Searle that, in order to obtain the removal of the GI warning from Celebrex's label, the study would have to treat patients out to at least 52 weeks. Ex. 17 (Loose Depo.) at 159-60; Ex. 18 at 161; Ex. 59 (Bowen Report) at 12 n.21. The FDA further stated that in order to claim that Celebrex had greater GI safety than traditional NSAIDs in general, it would have to prove individually safer than each of the comparator drugs used in the study. Ex. 59 (Bowen Report) at 12 nn. 22-23.

8. As agreed to by the FDA, CLASS was designed as two separate trials, one comparing Celebrex to ibuprofen and another comparing Celebrex to another NSAID called diclofenac. Ex. 113 (June 1, 2011 Expert Report of John Abramson, M.D. ("Abramson Report")) at 18; Ex. 63 at 7; Ex. 114 at 860. Each of the two trials

or "arms" of the CLASS study had a separate protocol that set forth how that trial would be conducted and how the data would be analyzed when the trial was complete. Ex. 113 (Abramson Report) at 18. Those protocols allowed patients taking low-dose aspirin for their hearts to participate in the study, even though aspirin is also known to cause GI problems. Ex. 114 at 878; Ex. 30 at 885. While the CLASS study was ongoing, the results were blinded, meaning that neither the investigators nor the patients knew who was taking Celebrex and who was taking one of the NSAIDs. Ex. 115 at 099; Ex. 116 at 140.

9. NSAIDs are known to cause symptomatic ulcers, which are ulcers accompanied by at least one symptom such as stomachache, as well as complicated ulcers, which are ulcers accompanied by either upper GI perforation, bleeding, or gastric obstruction in the stomach or intestines. Ex. 63 at 3. Complicated ulcers can – and most often do – occur without symptoms. Ex. 117 (July 14, 2011 Expert Report of Derek Patel, M.D. ("Patel Report")) at 13; Ex. 63 at 21.

10. Complicated ulcers are both rarer and more dangerous than symptomatic ulcers. Ex. 117 (Patel Report) at 8; Ex. 63 at 3. Although the CLASS study measured the prevalence of both complicated and symptomatic ulcers, the protocols stated that the rate of more serious complicated ulcers alone would determine whether Celebrex had greater GI safety. Ex. 118 at 616, 618; Ex. 119. Complicated ulcers were thus called the "primary endpoint," while symptomatic ulcers were of interest but were to have no bearing on the ultimate conclusion of the study. Ex. 118 at 616, 618. By

request of the FDA, the CLASS study also included a co-primary endpoint that measured the prevalence of complicated ulcers using an even more stringent, "alternate" definition. Ex. 114 at 881; Ex. 120 (July 7, 2011 Rebuttal Report of David Y. Graham, M.D. ("Graham Rebuttal")) at 15.

11. Searle planned to continue the CLASS trial until each patient had taken their assigned drug for at least six months and at least 20 ulcer complications had occurred in each of the two trials or 45 ulcer complications had occurred in both trials combined. Ex. 62 at 8. The longest a patient would be allowed to stay on medication in the trial was 52 weeks. Ex. 114 at 877. Accordingly, the clinical protocols for the CLASS trial stated that "[t]he Treatment Period is defined as the ***52-week*** interval during which study medication is taken or until the trial officially concludes, whichever occurs first." *Id.*; Ex. 121 at 961.

12. Once the study was complete, the protocols called for the results of the Celebrex patients in the two trials to be compared with the pooled results of the ibuprofen and diclofenac patients. Ex. 63 at 7. If Celebrex was safer than the pooled NSAIDs by a statistically significant margin, then the data would be analyzed to determine whether Celebrex was safer than ibuprofen and diclofenac individually. *Id.* Pursuant to the protocols, the CLASS study would only support a claim that Celebrex was safer than NSAIDs if it was statistically significantly safer in all three comparisons. *Id.*

The Conduct of the CLASS Study

13. CLASS was overseen by three committees of paid Searle consultants: the gastrointestinal events committee ("GEC"), the drug safety monitoring board ("DSMB"), and the executive committee ("EC"). Ex. 115 at 102, 113, 135. The GEC "adjudicated" GI events, meaning that they determined whether or not patients in CLASS had developed a complicated ulcer, while the DSMB monitored CLASS to ensure patient safety. *Id*. at 135. The EC supervised the other two committees and made recommendations to Searle regarding the conduct of the trial. *Id*.

14. The CLASS study started enrolling patients on September 23, 1998. Ex. 21 at 112. By the fall of 1999, the study had still not observed the required number of complicated ulcers. Ex. 115 at 127. Further, the rate of new complicated ulcers had slowed considerably. *Id*. Because the study was to continue until at least 20 ulcer complications occurred in each trial, on September 16, 1999, the committees extended the maximum length of the Celebrex/ibuprofen trial from one year to 15 months. *Id*.

15. On October 15, 1999, the CLASS data safety monitoring board for CLASS held another meeting. At that meeting, a presentation was made by Dr. William Zhao, an employee of Searle. *Id.* at 128; Ex. 122 (April 11, 2011 Deposition Transcript of William Zhao ("Zhao Depo.")) at 44-53. Dr. Zhao and one of the consultants "reviewed for the DSMB the discussion they had regarding the potential impact of a withdrawal rate greater than anticipated on the power of the study." Ex. 115 at 128.

16. By November 24, 1999, only 36 out of the 40 required ulcer complications had occurred in CLASS: 17 in the Celebrex/ibuprofen trial and 19 in the Celebrex/diclofenac trial. Ex. 116 at 166. Further, only a single ulcer complication had occurred in either trial in the previous two months. *Id*. Since it would likely take many more months for CLASS to reach the minimum 40 complicated ulcers required, Searle sent a November 24, 1999 letter to the FDA stating that it had decided to end the trial before 40 complicated ulcers had been observed. Ex. 16 (July 10, 2011 Rebuttal Report of Debra Bowen, M.D., FACAAI ("Bowen Rebuttal")) at 14 n.70.

17. On December 2, 1999, eight days after Searle had informed the FDA that it was ending the study prematurely, the three committees of consultants who supposedly oversaw the study also met and voted to terminate the study. Ex. 115 at 130. At the same meeting, which was attended by defendant Dr. G. Steven Geis ("Geis"), the draft minutes were reviewed of the October 15, 1999 DSMB meeting at which Dr. Zhao presented. *Id*.

18. On December 3, 1999, Searle representatives, including defendant Geis, met with the FDA. Ex. 123. At that meeting, and in the presence of defendant Geis, a Searle representative told the FDA that "Searle's only role at the open DSMB meetings was to record what transpired in the form of official meeting minutes." Ex. 123 at 024.

19. The Statistical Analysis Plan, which set forth in detail how the CLASS data would be analyzed, was finalized on December 7, 1999, after the decision had been made to halt the study. Ex. 118. The Statistical Analysis Plan did not describe any bias due to informative censoring or the truncation of the CLASS data at six months as a means of reducing any bias. *Id*.

The Results and Analysis of the CLASS Study

20. By the time it was finished, the CLASS study had cost at least $100 million. Ex. 79 at 804.

21. After finishing required patient follow-up and collecting the CLASS data, the study was unblinded on March 17, 2000. Ex. 124 at 653; Ex. 8 (December 10, 2010 Deposition Transcript of Pharmacia Vice President Steven Geis ("Geis Depo.")) at 30:11-15. At that time, the researchers could finally discern which patients were taking Celebrex and which NSAIDs, and immediately began analyzing the data. *Id*.

22. Concerned that CLASS might fail to prove a Celebrex GI safety advantage, the CLASS steering committee met from 8:30-10:00 a.m. on March 20, 2000 with defendant Geis in attendance. Ex. 19 at 816. Notes of that meeting state, "***[w]orst case: we have to attack the trial design if we don't see the results we want. Best case: Data is all we want and we go forward; will need to justify our trial***

design." *Id*.[3] The notes further state, "contingency plans are deliverable for tomorrow morning's meeting. . . . Contingency: primary endpoints do not deliver . . . ." *Id*.

23. As promised, on March 21, 2000, a PowerPoint presentation set forth the company's contingency plans. Ex. 20. One slide was entitled "Contingencies – Defend Celebrex Data." *Id*. at 524. According to that slide, if neither arm of CLASS showed a statistically significant advantage or "separation" for Celebrex, the plan was to "***[e]xplain through statistical glitches***." *Id*.

24. Another email from March 21, 2000, to defendant Geis states, "[a]s a contingency in case one arm in the CLASS trial doesn't separate, Mike C/Rich M to look into whether we can lump the CLASS data together and never show the separate arms." Ex. 125 at 486.

25. By the time the contingency plans were presented on March 21, 2000, defendant Geis and a few others had already learned the results of CLASS. Ex. 126 at 542. CLASS had failed. Exs. 21, 34, 36. Specifically, CLASS showed no statistically significant difference in ulcer complications between Celebrex and ibuprofen or diclofenac. Ex. 21 at 117 (Table 2). Because ulcer complications were the primary endpoint, the failure to show a significant advantage in such

---

[3] Unless otherwise noted, all emphasis is added throughout.

complications for Celebrex meant that Defendants[4] could not claim a GI safety advantage for Celebrex based on CLASS. Ex. 114 at 887.

26. In addition, the relative safety of Celebrex deteriorated as the study progressed, with Celebrex performing far worse after the first six months of the study than before. Ex. 1 (September 21, 2010 Deposition Transcript of *British Medical Journal* Author Peter Juni, M.D. ("Juni Depo.")) at 37-38 ("So it was striking that at six months there was quite a pronounced difference in favor of celecoxib and this entirely disappeared when you looked at the entire data available up to the maximum follow-up."); Ex. 23 (January 20, 2011 Deposition Transcript of Pfizer Medical Director Mitchell Gandelman ("Gandelman Depo.")) at 76:17-77:8 ("six-month data was more favorable to Celebrex than the 12-month or entire study data"); Ex. 24 (October 19, 2011 Deposition Transcript of Pharmacia Associate Medical Director for Rheumatology and Pain Emilio Arbe, M.D. ("Arbe Depo.")) at 84:15-85:5 (six-month data "created the false impression that based on this study, one could conclude that Celebrex was unique in its GI, gastrointestinal side effect profile"); *id.* at 323:9-326:7 ("the longer you go on to take these treatments, the less favorable the profile of Celebrex is"); Ex. 1 (Juni Depo.) at 52:20-53:9 ("the potential advantage of celecoxib over the two comparator drugs disappears over the second time window of seven to 12

---

[4] "Defendants" are Pharmacia, Pfizer, Geis, Fred Hassan ("Hassan"), and Carrie Cox ("Cox").

months and it disappears entirely"); Ex. 17 (Loose Depo.) at 168:7-10 ("the six-month data was more favorable to Celebrex than the entire study"); Ex. 2 (Weiner Depo.) at 184:17-25 ("six-month data was more favorable to Celebrex"); Ex. 8 (Geis Depo.) at181 ("the difference at 6 months looks wider than the difference at 12 months"); Ex. 21 at 117-18 (Tables 1-4).

27. Indeed, the post-six-month results for Celebrex were dismal: six of the seven complicated ulcers occurring after the first six months of the trial were suffered by patients being treated with Celebrex. Ex. 24 (Arbe Depo.) at 315:18-316:16 ("six of the seven CSUGIEs suffered during the class trial after six months occurred in the Celecoxib treatment group"); Ex. 21 at 117-18 (Tables 1-4).

28. Similarly, Celebrex showed a statistically significant reduction in complicated ulcers at six months among patients who did not take aspirin, but that advantage did not hold for the full duration of the study. Ex. 66 at 117-18 (Tables 1-4); Ex. 39 (November 11, 2010 Deposition Transcript of Pharmacia Chief of Research and Development Dr. Goran Ando ("Ando Depo.")) at 157:4-158:5 ("showing of statistical significance did not hold "for the entire study period"); Ex. 17 (Loose Depo.) at 84:25-85:7 ("for the entire study you could not claim statistical significance in the comparison for non-aspirin users for complicated ulcers between Celebrex and the two NSAIDs combined"); Ex. 24 (Arbe Depo.) at 332:16-334:18 ("finding of a statistical significance" did not hold "for the entire study period"); Ex. 2 (Weiner

Depo.) at 72:1-13 ("that finding of statistical significance does not hold for the entire study period").

29. At neither six months nor the entire study duration did the CLASS study show any statistically significant difference between Celebrex and diclofenac on any of the eight GI endpoints considered. Ex. 21 at 117-18 (Tables 1-4); Ex. 8 (Geis Depo.) at 137:8-23 ("You can't say on any of these eight endpoints, that the comparison between Diclofenac and Celebrex was statistically significant . . . ."); Ex. 39 (Ando Depo.) at 177:7-12 ("Celebrex did not separate from Diclofenac"); Ex. 24 (Arbe Depo.) at 321:2-323:8 (none of the eight comparisons are statistically significant); Ex. 1 (Juni Depo.) at 28:13-29:2 ("It reveals that there were – there was no statistical evidence for a benefit of celecoxib as compared with diclofenac . . . ."); Ex. 2 (Weiner Depo.) at 143:20-25 ("diclofenac and celecoxib are no different with respect to any of the eight measures addressed in Exhibit 115, the final report"); Ex. 127 at 726 ("diclofenac ulceration rate . . . was no different than celebrex"); Ex. 128 at 332 ("CLASS study attempted to differentiate from diclofenac but failed.").

30. In fact, Celebrex performed worse than diclofenac on the FDA-mandated co-primary endpoint of the study. Ex. 21 at 156-58; Ex. 69 at 312; Ex. 17 (Loose Depo.) at 89:4-8 ("the event rate for celecoxib is approximately twice that which it was for diclofenac" for the FDA alternative definition of complicated ulcer); Ex. 1 (Juni Depo.) at 28:13-29:2 ("according to the more stringent alternate definition that was required by the FDA, there was even a nonsignificant trend in favor of diclofenac

as compared to celecoxib"); Ex. 2 (Weiner Depo.) at 79:8-12 ("the celecoxib alternative definition of CSUGIE event rate is nearly double that of diclofenac").

31. Even though it "missed" statistical significance at the .05 threshold, the p-value of .09 reported by Defendants for the primary end point, overstated the safety of Celebrex as the actual p-value was .45. Ex. 21 at 117.

32. There was not a 91% chance Celebrex was safer than the comparator drugs, as the p-value reported by Defendants claimed, but in fact the drugs were basically no different, as a p-value of .45 indicates. Ex. 72 (May 13, 2011 Expert Report of Nicholas P. Jewell, Ph.D. ("Jewell Report")) at 10-14.

Defendants' Internal Dissemination of the CLASS Study Results and the Pharmacia/Searle Merger

33. Defendant Geis and his team created a slide deck dated March 23, 2000 entitled "[t]he bottom line" that reported:

- The post-six-month CLASS results were less favorable for Celebrex than the first six months of results;
- Celebrex's statistically significant safety advantage for complicated ulcers among non-aspirin takers did not hold for the entire study period; and
- Celebrex showed no GI safety advantage over diclofenac in CLASS.

Ex. 34 at 480-81, 500, 518; Ex. 35 at 874-75, 897. These same results were reiterated in two more slide decks created by Geis's team dated March 28 and April 3, 2000. Exs. 36-37.

34. Searle, which was a subsidiary of Monsanto, merged with Pharmacia on March 31, 2000. Ex. 129 at 2. On that same day, Geis's team disseminated the CLASS results to Pfizer "R & D leadership." Ex. 36 at 864; Ex. 100 at 898.

35. Pfizer was informed of the full CLASS results in late March or early April, 2000. Ex. 130; Ex. 100 at 898; Ex. 8 (Geis Depo.) at 41-42; Ex. 131 at 974; Ex. 17 (Loose Depo.) at 61:16-64:5 (Pfizer received the CLASS data at a March 23, 2000 meeting); *id.* at 24-25 ("The Operations Committee would have received the results of the CLASS study shortly after it was unblended . . . ."); *id.* at 71:4-11 (Pfizer "became aware shortly after the data was unblinded that there was a statistically significant difference for the non-aspirin group at six months, but there was not a statistically significant difference in the comparison at twelve months"); Ex. 36 at 864.

36. On April 7, 2000, the CLASS results were disseminated to Searle/Pharmacia "commercial leadership." *Id.*; Ex. 100 at 898.

37. In early April of 2000, defendant Geis presented the CLASS study results to defendants Hassan and Cox, including the post-six-month data. Ex. 8 (Geis Depo.) at 38-40; 173-74; Ex. 38 (February 22, 2011 Deposition Transcript of CEO of Pharmacia Fred Hassan, Vols. I-II ("Hassan Depo.")) at 20:8-12.

38. Hassan and Cox also both sat on the Executive Management Committee ("EMC"), which was made aware of the CLASS results. *See, e.g.*, Ex. 17 (Loose Depo.) at 22-25; Ex. 2 (Weiner Depo.) at 231-32; Ex. 41 at 709.

39. Hassan and Cox did not object to the publication of only the six-month data. Ex. 8 (Geis Depo.) at 170-74.

40. On April 30, 2000, Pfizer received a draft of the Final Study Report which contained all the salient CLASS data. Ex. 132 at 825-26 (Tables 1-4).

41. Defendants did not provide the consultants that served on the committees that oversaw the CLASS study – and who would serve as authors of the *Journal of the American Medical Association* ("JAMA") article – with the full results of the study. Ex. 8 (Geis Depo.) at 308:6-10.

Defendants Manipulated the CLASS Study Results to Favor Celebrex

42. On March 21, 2000, Geis ordered 15 separate analyses of the CLASS data conducted. Ex. 126 at 542-43. Per Geis's instructions, Searle looked at ulcer complications at six months, but there was no significant difference at that point either. Ex. 21 at 117 (Table 1). Geis's team was only able to manufacture a statistically significant difference in ulcer complications between Celebrex and both NSAIDs by cutting off the study at six months and by excluding the 22% of patients who took aspirin during the study. *Id*.

43. Geis decided to perform the six-month only after seeing the results. Ex. 133; Ex. 134 at 809 ("we did not identify 6 months as an appropriate analysis until after the study was unblinded"). As Emilio Arbe, an Associate Medical Director at Pharmacia, stated in an email, "***[w]ith a bit of data massage, what Steve Geis and his team have done is to focus on the 6 month data, for no other reason that it happens***

to look better." Ex. 11 at 477. Similarly, Mona Wahba ("Wahba"), a Medical Director at Pfizer, later wrote an email that stated, "***[w]e are also cherry picking the data (using 6m as study duration***)." Ex. 12 at 695.

44. Geis's team also tried adding symptomatic ulcers to the comparison. Symptomatic ulcers are not associated with complications such as upper GI perforation, bleeding, or gastric obstruction, and are less serious and much more common than complicated ulcers. Ex. 21 at 117-18, 136-37. By adding 67 symptomatic ulcers to the 38 complicated ulcers observed in CLASS, Geis's team created a comparison that resulted in statistical significance. *Id*. at 117 (Table 2), 118 (Table 4). This comparison was not planned, however, until after Geis and his team had seen the results of the study. Ex. 114 at 887; Ex. 133.

Defendants' Public Dissemination of the CLASS Results

45. On March 17, 2000, defendant Cox made an internal presentation that spelled out the "Celebrex – ***CLASS Update: Rollout Schedule***." Ex. 44 at 030; Ex. 45; Ex. 46 (February 9, 2011 Deposition Transcript of President of Pharmacia Carrie Cox ("Cox Depo.")) at 38. One slide in this presentation specifically described the press releases and presentations about CLASS that would be issued in April and May of 2000. *Id*.

The April 15, 2000 Presentation of the CLASS Study Results at the American College of Physicians Meeting

46. Geis and his team created draft versions of the initial public presentation of the CLASS data for use at the April 15, 2000 American College of Physicians ("ACP") meeting in Philadelphia. Ex. 135; Ex. 8 (Geis Depo.) at 66-67. At least one draft of this presentation that was circulated to Pharmacia and Pfizer executives included the omitted 12-month data. Ex. 136.

47. On April 15, 2000, Dr. Fred Silverstein, a Pharmacia-paid consultant, presented the results from the first six months of CLASS at the ACP meeting in Philadelphia. Ex. 22. The slides Dr. Silverstein presented at ACP made no mention of post-six-month data. Exs. 137-138.

48. On April 24, 2000, The Pink Sheet, a pharmaceutical industry newsletter published an article about CLASS. Ex. 139. The article states, "[d]ata from the first six months of the trial were used for the head-to-head comparison of NSAIDs because patients were not required to remain on their assigned drug after the six months, study investigator Fred Silverstein, MD, University of Washington, explained." *Id*. at 2. The article makes no mention of informative censoring or any other bias that would warrant the exclusion of post-six-month data from CLASS. *Id*.

Defendants' April 17, 2000 Press Release

49. On April 17, 2000 – the first day of the Class Period – Pharmacia and Pfizer issued a joint press release announcing the results of CLASS. Ex. 22; Ex. 2 (Weiner Depo.) at 84:5-25; Ex. 17 (Loose Depo.) at 12:20-14:2.

50. Pfizer executives received drafts of the press release to comment on before it was published. Exs. 95-96; Ex. 17 (Loose Depo.) at 12:20-13:4, 13:13-14:2.

51. Pfizer Chief Medical Officer Joe Feczko approved the CLASS press release. *See* Ex. 17 (Loose Depo.) at 12:20-14:2.

52. The Pfizer/Searle "U.S. Collaboration Agreement (Celecoxib)" stated that "[n]either party shall originate any news release or other public announcement, written or oral, relating to this Agreement without the prior written approval of the other party except as otherwise required by Law." Ex. 93 at 113.

53. "Pharmacia corporate management" also reviewed and approved the press release, including defendant Geis, Pharmacia's Executive Vice President, Al Heller ("Heller"), Chief Scientific Officer Philip Needleman, Ph.D. and Senior Executive Vice President Richard De Schutter ("De Shutter") ((*see* Ex. 140 at 962)). Exs. 94, 97, 141.

54. The press release was also approved by Pharmacia's regulatory affairs committee before publication. Ex. 97. Defendant Geis reviewed no fewer than three drafts of this press release before it was issued. Exs. 94 (April 7, 2000 draft), 95-96

(April 11, 2000 draft, with different cover emails), 97 (April 14, 2000 draft), 22 (final).

55. According to the "Global Agreement Among Pfizer Inc., Monsanto Company and G.D. Searle & Co.," dated February 18, 1998 "[t]he EMC shall have the final decision making authority with respect to all matters within the jurisdiction of any of the Committees established pursuant to this Article 3 or pursuant to one of the other Agreements which are referred to the EMC for determination or remain unresolved in the CSC, OpCom or other Committee." Ex. 14 at 922. Cox testified that she had authority to review product-specific press releases. Ex. 46 (Cox Depo.) at 30:20-31:21.

56. The press release characterized CLASS as a "13-month" study. Ex. 22 at 977. The press release did not disclose that the results presented therein were based upon only the first six months of the study or that the results after six months were less favorable to Celebrex. Ex. 22.

57. The press release stated that "Celebrex was also associated with numerically fewer ulcer complications than the NSAID comparators among all patients, and 64 percent fewer of these serious events among non-aspirin users – ***a statistically significant difference***." *Id*. at 978. The press release did not disclose that this comparison was based only upon the first six months of the study and was not statistically significant for the entire study period.

58. The press release also stated that "Celebrex patients experienced significantly fewer symptomatic GI ulcers and ulcer complications compared with ibuprofen or diclofenac." *Id*. The press release did not disclose that Celebrex patients did not in fact suffer significantly fewer symptomatic and complicated ulcers compared with diclofenac at six months or for the entire study period. Ex. 22.

59. J.P. Morgan published an analyst report on April 17, 2000, which stated:

- . . . [R]esults of the Celebrex (Pharmacia) CLASS trial (on GI events vs. NSAIDs) were presented Sat. night (April 15).
- On a variety of measures, Celebrex showed clear statistical superiority on GI safety versus NSAIDs . . . .

* * *

We expect meaningful modification of the standard NSAID GI warning . . . .

Ex. 108 at 1-2.

60. Defendants knew that the CLASS data would not support a modification of the NSAID GI Warning by the FDA. Ex. 27 at 679. ("data won't support the original intent of modify[ing] the GI warning . . . ."); Ex. 142 ("Previous discussions with management regarding potential labeling scenarios once the CLASS data was available included an option to remove the GI warning. . . . Based on the results of the trial, this approach no longer seems appropriate."); Ex. 143 (Weiner email dated April 8, 2001 – "The warning looks at present just like, if not worse than, the standard

NSAID GI warning. This was what I was afraid of as soon as we knew we didn't make our primary endpoint.").

61. Between April 17 and April 19, 2000, Pharmacia's stock price increased from $53.13 per share to $59.75. Ex. 6 (June 6, 2011 Report on Market Efficiency, Loss Causation, and Damages, Steven P. Feinstein, Ph.D., CFA ("Feinstein Report")) at 12.

Defendants' April 25, 2000 Analyst Conference Call

62. On April 25, 2000, Pharmacia management, including defendants Geis, Hassan, and Cox, held a conference call with financial analysts. Ex. 15.

63. During the call, defendant Hassan stated that "[w]ith Celebrex, we now have exciting new data that shows that Celebrex has a truly exceptional safety profile. This makes us feel good at a time when other products have been affected by safety concerns. . . . . We are . . . very pleased with the CLASS data . . . ." *Id.* at 348, 357.

64. During the call, Pharmacia Executive Vice President Heller stated that "Celebrex resulted in 42% fewer symptomatic ulcers and ulcer complications versus the NSAID comparators, a statistically significant difference. Among non-aspirin users, the difference was 53% in favor of Celebrex, also statistically significant. When we focus only the most serious GI events, mainly ulcer complications which include perforations, gastric obstructions and GI bleeds, among all patients including those using low-dose aspirin, Celebrex resulted in 52% fewer ulcer complications, a finding that was just under statistical significance. Among non-aspirin users, the

difference was 65%, which was ***statistically significant***." *Id.* at 352. No one on the call disclosed that these results were based only upon six months of data from the CLASS study, that the results were less favorable for Celebrex over the entire study period, or that the statistically significant result for non-aspirin users was not statistically significant over the entire study period.

65. During the call, Heller also stated that "[t]he top line take-away is that our landmark long-term arthritis study provides compelling evidence of the broad safety profile of Celebrex across a full spectrum of GI measures and in major organ systems versus the traditional NSAID comparators ibuprofen and diclofenac. . . . We look forward to presenting a fully analyzed data . . . from this trial to the FDA before mid-year." *Id*. at 352-53.

Defendants' May 23, 2000 Press Release

66. On May 23, 2000, Pharmacia had a paid consultant, Dr. Jay Goldstein, present the six-month CLASS results at the Digestive Disease Week conference in San Diego, California. Ex. 28.

67. On the same day, Pharmacia and Pfizer issued another joint press release announcing the presentation. *Id*. The press release again characterized CLASS as a "13-month" study and claimed that Celebrex patients in CLASS who did not take aspirin suffered statistically significantly fewer ulcer complications than non-aspirin takers on NSAIDs. *Id*. at 2, 4-5. The press release did not disclose that this result was only significant at six months and did not hold at for the entire study period. Ex. 28.

Regarding the Digestive Disease Week presentation, Pfizer Clinical Research Assistant Samuel Zwillich, M.D. wrote an email that "[t]hey swallowed our story, hook, line and sinker." Ex. 29 at 751.

The June 25, 2000 Meeting of the Cox-2 Inhibitors Clinical Safety Committee

68. On June 25, 2000, Pharmacia's Cox-2 Inhibitors Clinical Safety Committee met in Rosemont, Illinois. At that meeting, the committee observed that when presenting the results of the CLASS study, the company should "***make clear when results are presented for data truncated at 6 months***." Ex. 144 at 740.

The JAMA Article

69. Pharmacia recruited ten paid consultants to serve as authors of the JAMA article, along with six Pharmacia employees, including defendant Geis. Ex. 30 at 878. Geis was listed as the senior author of the article. Ex. 145 (August 6, 2010 Deposition Transcript of Pharmacia Scientist Kenneth Verburg ("Verburg Depo.")) at 234:15-235:3; Ex. 30. Dr. James Lefkowith, a Pharmacia employee, circulated a first draft of the article to the consultant/authors who in turn provided him with their comments and suggestions. Ex. 13 (September 29, 2010 Deposition Transcript of JAMA Author Fred Silverstein, M.D. ("Silverstein Depo.")) at 156.

70. Dr. Lee Simon, one of the consultant/authors of the JAMA article and a member of the CLASS EC, suggested to Dr. Lefkowith that the article state that patients in the study had a mean duration of drug exposure of nine months. Ex. 146 at 276; Ex. 49 (September 16, 2010 Deposition Transcript of Pharmacia Consultant and

JAMA Author Lee Stuart Simon ("Simon Depo.")) at 114:1-13. This suggestion was not adopted. Ex. 30.

71. Robert Makuch, Ph.D., another consultant/author of the JAMA article, made the following written suggestion regarding the manuscript: "***I think reviewers and readers will want to have all data, not just 6 mos*** . . . ." Ex. 48 at 378. Again, this suggestion was disregarded. Ex. 30.

72. Dr. Silverstein, the first author of the JAMA article and the chairman of the EC which ran the CLASS study, told defendant Geis that the article should include a section disclosing the existence of the post-six-month CLASS results and any reasons for focusing on the six-month results. Ex. 13 (Silverstein Depo.) at 157:3-25. Defendant Geis told Dr. Silverstein that he agreed with him and that he would have the section added to the manuscript before it was submitted to JAMA. *Id*. The disclosure Dr. Silverstein requested was drafted, but it was not included in the final manuscript. Exs. 30, 147. Dr. Silverstein did not learn that the requested disclosure was omitted, however, until he read the final article after it was published. Ex. 13 (Silverstein Depo.) at 166:25-167:9.

73. Dr. Mitchell Gandelman, a Vice President and Medical Director at Pfizer, also recommended that the JAMA article disclose the existence of post-six-month results and the rationale for focusing on the first six months. Ex. 23 (Gandelman Depo.) at 70:4-11, 71:11-13.

74. A draft of the JAMA manuscript prepared prior to the unblinding of the CLASS data accurately described the study as lasting "65 weeks." Ex. 148. Drafts created after the data was unblinded were changed to state the study lasted "6 months" (Ex. 149), or "at least 6 months" (Ex. 150). The final publication told readers that the study lasted "6 months" and that all participants completed "a minimum of 6 months of treatment." Ex. 30 at 879. Another document demonstrates that CLASS manuscript authors considered inserting a statement explaining that the article was based only on the first half of the study data, but ultimately they did not. Ex. 147. This caused one internal author to worry, "[i]f someone criticizes us mixing up 6-month and study, are we covered?" Ex. 151 at 412. Pfizer reviewed the JAMA manuscript before it was submitted. Ex. 101 at 367.

75. JAMA specifically asked the JAMA authors whether they had more than six months of data from CLASS and they responded that it was a six-month study and that the study was closed. Ex. 9 (January 12, 2007 Deposition Transcript of Editor and Chief of JAMA Catherine De Angelis ("De Angelis Depo.")) at 26:24-27:12.

76. JAMA provided a "Checklist for Authors Submitting Reports of Randomized Controlled Trials to JAMA" to the JAMA article authors. That checklist provided that authors were to "[s]tate specific interpretation of study findings, including sources of bias." Ex. 32 at 091.

77. Defendants submitted a finalized manuscript of the JAMA article on or around June 20, 2000. Ex. 152; Ex. 153 at 085; Ex. 122 (Zhao Depo.) at 121:24-

123:20. This submission did not include any of the post-six-month CLASS results or any reason for omitting those results from the article. Ex. 2 (Weiner Depo.) at 276:20-23; Ex. 17 (Loose Depo.) at 137:17-138:2; Ex. 145 (Verburg Depo.) at 97:6-14; Ex. 31 at 2399.

78. After the JAMA manuscript was submitted but before it was published, an internal Pharmacia email was forwarded to Dr. Lefkowith, the Pharmacia employee in charge of drafting the article, regarding the manuscript. The email stated, "[t]he paper does not report the results for the two NSAIDs separately (when in fact they are very different) . . . [t]here is no discussion in the paper about the likely bias introduced by the differential drop-out in the two groups." Ex. 154 at 353. After reviewing these comments, one Pfizer executive observed, "[i]t appears that there are discrepancies between the JAMA manuscript for CLASS and the CLASS study report. . . . It seems likely that this discrepancy will emerge during the NICE [England's National Institute for Health and Clinical Excellence] review . . . ." Ex. 155 at 714.

79. The JAMA article was published on September 13, 2000. Ex. 30; Ex. 33 at 826.

80. The article stated that the objective of the CLASS study was "[t]o determine whether celecoxib, a COX-2-specific inhibitor, is associated with a lower incidence of significant upper GI toxic effects and other adverse effects compared with conventional NSAIDs." Ex. 30 at 878.

81. The article stated that the CLASS study's main outcome measure was "[i]ncidence of prospectively defined symptomatic upper GI ulcers and ulcer complications (bleeding, perforation, and obstruction) and other adverse effects during the 6-month treatment period." *Id*.

82. The article reported a statistically significant result for complicated ulcers in patients not taking aspirin. *Id.* at 878, 882 (Figure 2B). It did not disclose that this comparison was not statistically significant for the entire study period.

83. Regarding ulcer complications among all patients, the article reported a p-value of 0.09. *Id.* at 878. It did not report that this p-value for the entire study period was 0.45. Ex. 30.

84. The article stated "[i]n this study, celecoxib [Celebrex], at dosages greater than those indicated clinically, was associated with a lower incident of symptomatic ulcers and ulcer complications combined, as well as other clinically important toxic effects, compared with NSAIDs at standard dosages." *Id.* at 878.

85. The article stated "[t]his study determined that celecoxib [Celebrex], a COX-2-specific inhibitor, when used for 6 months in a dosage 2 to 4 times the maximum therapeutic dosage, is associated with a lower incidence of combined clinical upper GI events than compared to NSAIDs (ibuprofen and diclofenac) used at standard therapeutic dosages." *Id*. at 884-85.

86. The article stated "our results demonstrate that celecoxib, at a dosage 2- to 4-fold greater than the maximum therapeutic dosages and those approved for

labeling for RA and OA, is associated with a lower rate of upper GI toxic effects compared with standard therapeutic dosages of NSAIDs. This finding supports the COX-2 hypothesis that COX-2 – specific agents exhibit decreased GI toxic effects." *Id*. at 885.

87. The article did not disclose that the study showed no statistically significant advantage for Celebrex over one of the two traditional NSAIDs studies in CLASS – diclofenac – for any GI endpoint at six months or for the entire study period.

88. The article also did not disclose that the CLASS study showed diclofenac to be numerically safer than Celebrex using the more stringent endpoint requested by the FDA. Ex. 30.

Defendants' September 13, 2000 Press Release

89. On September 13, 2000, Pharmacia and Pfizer issued a press release regarding the JAMA article that stated: "A newer medication used to treat arthritis appeared to have fewer deleterious side effects than the traditional therapies studied, according to a study published in the Sept. 13 issue of the Journal of the American Medical Association (JAMA)." Ex. 33 at 826.

90. The press release stated "This is good news for arthritis patients seeking a safe and effective option for treating this chronic condition, which requires them to take medication indefinitely,' said Dr. Jay Goldstein, professor of medicine at the University of Illinois at Chicago, a study author and chair of the Gastrointestinal

Events Committee. 'The news is especially significant because many arthritis patients are unable to use and often have to discontinue traditional therapies because of gastrointestinal or other side effects.'" *Id*.

91. The press release stated "[c]ompared with traditional nonsteroidal anti-inflammatory agents, Celebrex has been shown to effectively manage the pain and inflammation of arthritis, while reducing the potential for ulcer complications and other serious side effects that can lead to hospitalization and even death,' said Dr. Goldstein. 'This is particularly important because 60 to 80 percent of gastrointestinal complications from nonsteroidal anti-inflammatory drug use occur without previous symptoms.'" *Id.* at 827.

The September 13, 2000 JAMA Editorial

92. On September 13, 2000, an editorial authored by M. Michael Wolfe M.D. and David R. Lichtenstein, M.D. was published in JAMA accompanying the CLASS journal article referenced above. The editorial states: "In this issue of THE JOURNAL, Silverstein et al. report the results of a ***6-month*** randomized, double-blind, controlled trial comparing the ulcerogenic potential and upper GI toxicity of celecoxib in individuals with osteoarthritis (OA) and rheumatoid arthritis (RA)." Ex. 156 at 001.

93. Before the Wolfe and Lichtenstein editorial was published, several Pharmacia employees reviewed a draft containing the characterization of CLASS as a "6-month" study. Ex. 157. None of those employees alerted Dr. Wolfe, JAMA, or

anyone else that the description of CLASS in the editorial was incorrect. Ex. 23 (Gandelman Depo.) at 150:13-151:17, 190:7-193:4.

94. Instead, on September 8, 2000, one employee wrote in an internal email to colleagues, "[c]learly this editorial might be more important than the actual publication. . . . Countries need to be trained in both pieces our study pub. AND this editorial." Ex. 157 at 370.

95. After the editorial was published, two of the authors of the JAMA article read it and knew its characterization of the CLASS study to be inaccurate, but did not seek to correct it. Ex. 49 (Simon Depo.) at 160:23-161:19; Ex. 26 (July 27, 2010 Deposition Transcript of Pharmacia Consultant and JAMA Author Gerald Faich ("Faich Depo.")) at 226:7-229:6.

96. After the JAMA article was printed, Pharmacia and Pfizer ordered hundreds of thousands of reprints of the JAMA article and distributed them to doctors for promotional purposes. Ex. 69 at 313; Ex. 92 at Nos. 1-2.

97. The first page of the JAMA article which Defendants disseminated directs readers to the Wolfe and Lichtenstein editorial. Ex. 30 at 878.

Dr. Needleman's September 14, 2000 Presentation to Investors

98. On September 14, 2000, Dr. Needleman, the Chairman of Pharmacia's research and development, gave a presentation to the Bear Stearns Healthcare Conference. Ex. 110. At that conference, Dr. Needleman told investment analysts that "we are very excited about the filing of the sNDA for the long-term safety of

Celebrex and ***we are confident that FDA will also find this data compelling***. ***Removal of the NSAID class GI warning will open the door to increased prescribing of Celebrex*** – including some managed care formularies which have favored generic NSAIDs based on price alone." *Id.* at 499.

October 25, 2000 Internal Pharmacia Email

99. On October 25, 2000 an email from Pharmacia's European operations was forwarded to Dr. Lefkowith, the Pharmacia employee in charge of drafting the JAMA article. Ex. 158. That email stated, "the draft document states that the CLASS study results establish conclusively that [Celebrex] is associated with a significantly lower incidence of symptomatic ulcers and ulcer complications than NSAID comparators – this is a very absolute statement. I do not see how the data support this statement or other similar ones." *Id.* at 211.

Defendant Cox's October 25, 2000 Presentation of the CLASS Study Results

100. On October 25, 2000, defendant Cox presented the CLASS results at the CIBC World Markets Health Care Conference. Ex. 43. Cox's presentation stated that CLASS showed a statistically significant reduction in complicated ulcers for non-aspirin users taking Celebrex. *Id.* at 407. It did not disclose that this result was based upon only six months of study data or that the comparison was not statistically significant over the entire study period. *Id.* Cox's presentation also referred the audience to the JAMA article. *Id.*

Defendant Hassan's February 6, 2001 Presentation of the CLASS Study Results

101. On February 6, 2001, defendant Hassan presented the CLASS study results at the Merrill Lynch Global Pharmaceutical, Medical Device & Biotechnology Conference. Ex. 42. Hassan's presentation referred the audience to the JAMA article and claimed "48%-66% reduction in ulcer complications." *Id*. at 626. It did not disclose that these results were based upon only six months of study data or that the percentages were less favorable for Celebrex when using data from the entire study period. *Id*.

Defendants Did Not Publicly Disclose Unfavorable Data from the CLASS Study

102. Prior to February 6, 2001, Defendants had not informed investors that the post-six-month results from the CLASS study were less favorable to Celebrex than the six-month results that Defendants had published. Exs. 15, 22, 28, 30, 33, 42-43, 110, 137, 159; Ex. 2 (Weiner Depo.) at 184:17-25 (prior to February 7, 2001 "publicly the company had focused on the six-month data . . . [a]nd that six-month data was more favorable to Celebrex"); Ex. 1 (Juni Depo.) at 52:20-53:9 (Defendants failed to disclose that "the potential advantage of celecoxib over the two comparator drugs disappears over the second time window of seven to 12 months and it disappears entirely."); Ex. 8 (Geis Depo.) at 151-52 (The April 17, 2000 press release "presents what Dr. Silverstein presented. Dr. Silverstein presented this 6-month analysis."); Ex. 37 at 585 ("Publication Strategy" specified the release of only the "6 month

efficacy/general safety & labs."); Ex. 9 (De Angelis Depo.) at 88-89 ("the JAMA article was misleading for failing to acknowledge the existence of post six-month data").

103. Prior to February 6, 2001, Defendants had not informed investors that 85% of the complicated ulcers occurring after six months were suffered by patients being treated with Celebrex. Exs. 15, 22, 28, 30, 33, 42-43, 110, 137; Ex. 24 (Arbe Depo.) at 315:18-316:16 ("the JAMA article, which has been marked as Exhibit 3" does not disclose that "six of the seven CSUGIEs suffered during the class trial after six months occurred in the Celecoxib treatment group"); Ex. 17 (Loose Depo.) at 83:25-84:6 (Defendants did not disclose that "six of the seven complicated ulcers experienced in the second six months of the trial were experienced in the celecoxib treatment group").

104. Prior to February 6, 2001, Defendants had not informed investors that the statistically significant reduction in complicated ulcers for Celebrex users not taking aspirin that Defendants reported based upon six months of data did not hold for the entire study period. Exs. 15, 22, 28, 30, 33, 42-43, 110, 137; Ex. 24 (Arbe Depo.) at 332:16-334:18 (Defendants did not disclose that "finding of a statistical significance" did not hold "for the entire study period"); Ex. 17 (Loose Depo.) at 135:7-12 ("the article does not disclose that that comparison would not hold for the entire study period").

105. Prior to February 6, 2001, Defendants had not informed investors that CLASS showed no statistically significant advantage compared to one of the two comparator drugs – diclofenac – on any ulcer comparison. Exs. 15, 22, 28, 30, 33, 42-43, 110, 137; Ex. 24 (Arbe Depo.) at 321:2-323:8 (no disclosure in JAMA article (Ex. 30) "that there is no difference with Diclofenac individually per the class data"); Ex. 1 (Juni Depo.) at 30:9-31:13 (this fact was not "reported in the JAMA article which has been marked as Wolfe Exhibit 3"); *id*. at 76:11-17 (failure to disclose equivalence of Celebrex and diclofenac rendered the JAMA article misleading); Ex. 17 (Loose Depo.) at 138:15-24 (JAMA article Ex. 30 "doesn't disclose that none of the eight comparisons listed in Tables 1 through 4 with respect to a comparison between Celebrex and diclofenac were statistically significant"); Ex. 8 (Geis Depo.) at 124:12-125:8 ("That analysis, comparing Celebrex for the combined endpoint of symptomatic ulcers and ulcer complications versus Diclofenac is not referenced here.").

106. Prior to February 6, 2001, Defendants had not informed investors that CLASS showed diclofenac to be numerically safer than Celebrex on the more stringent endpoint requested by the FDA. Exs. 15, 22, 28, 30, 33, 42-43, 110, 137; Ex. 1 (Juni Depo.) at 28:13-31:13 ("according to the more stringent alternate definition that was required by the FDA, there was even a nonsignificant trend in favor of diclofenac as compared to celebrex" that was not "reported in the JAMA article which has been marked as Wolfe Exhibit 3"); Ex. 17 (Loose Depo.) at 89:4-8, 137:10-17 (the JAMA article (Ex. 30) does not disclose that "the event rate for

celecoxib is approximately twice that which it was for diclofenac" for the FDA alternative definition of complicated ulcer).

Testimony of Pharmacia Medical Director Dr. Arbe that Defendants Statements Were Misleading

107. Pharmacia Associate Medical Director for Rheumatology and Pain Dr. Arbe testified as follows:

> Q. Did you believe – did you think that the way the company was trying to use the data, that is, the six-month data, was false and misleading in any way?
>
> A. Yes, I did.
>
> Q. And tell me why that – why you thought that.
>
> A. Because it created the false impression that based on this study, one could conclude that Celebrex was unique in its GI, gastrointestinal side effect profile, and looking closer at the data, I could not arrive at the same conclusion that this gave proof that this was the case.

Ex. 24 (Arbe Depo.) at 84:15-85:5.

108. Dr. Arbe further testified:

> Q. And what did you conclude in looking at the data?
>
> A. I concluded that we were being misleading in the way we were representing this study in public.

Id. at 58:3-7.

109. Dr. Arbe further testified:

> Q. And was the 12-month data, which is reported here in Table 2, was that incorporated into the JAMA manuscript, which is Plaintiffs' Exhibit 3?
>
> A. It wasn't, and it would have been clinically relevant.

Q. And in your opinion as a medical doctor, would it have affected your decisions with respect to whether or not to prescribe Celecoxib?

* * *

A. Yes, it would have influenced my decision.

Q. And the failure to include that information, your opinion, was that proper?

A. No, to me that was improper.

Q. And in your opinion, did it render the article misleading?

* * *

A. I think it made the article misleading.

Id. at 325:4-326:7.

Testimony of *British Medical Journal* Author, Dr. Peter Juni, that Defendants' Statements Were Misleading

110. *British Medical Journal* ("BMJ") author Dr. Peter Juni testified:

Q. And what does that mean, that it decreases?

A. And that the potential advantage of celecoxib over the two comparator drugs disappears over the second time window of seven to 12 months and it disappears entirely.

Q. And is that disclosed in the JAMA article?

A. No, unfortunately not.

Q. And does that render the JAMA article misleading?

A. Yes.

Ex. 1 (Juni Depo.) at 52:20-53:9.

111. Dr. Juni further testified:

Q. – was Wolfe Exhibit 3 misleading?

A. Wolfe Exhibit 3 was a misleading representation of the results of the two CLASS studies, yes.

Id. at 91:8-11.

112. Dr. Juni further testified:

Q. And was the equivalence of diclofenac and celecoxib disclosed in the JAMA article, Wolff Exhibit 3?

A. No.

Q. And did it render that article misleading?

A. Yes.

Id. at 76:11-17.

113. Dr. Juni further testified:

Q. And you write at the bottom of the first page of Exhibit 32 your British Medical Journal editorial, quote, "Almost all of the ulcer complications that had occurred during the second half of the trials were in the users of celecoxib." Is that an accurate statement?

A. That is – there were, if I remember that correctly, seven ulcer complications that were not censored, that were included in the principal analysis as submitted to the FDA.

Six of these were in celecoxib arms and one of them was in a comparator arm, if I remember correctly. Let me just check whether this is right. This was in the – probably in the ibuprofen arm, but I couldn't be sure whether it was in the ibuprofen or in the diclofenac arm, but six versus one.

Q. And was the information disclosed in the JAMA article, Wolfe Exhibit 3?

A. No.

Q. And did that render the article misleading.

A. This was one of the parts that rendered the article misleading. I was already referring the article misleading. I was already referring to two others, but there is one more that was quite problematic in my view.

Id. at 46:2-47:5.

Testimony of Pfizer Medical Director Dr. Gandelman

114. Pfizer Medical Director, Dr. Gandelman testified:

Q. And the, clearly somebody, from – from your notes here, you're – you're – you're communicating either your thoughts or somebody else's thoughts that the failure to disclose the full 12-month data in the JAMA article raised ethical concerns.

Is that an accurate way of reading your notes?

* * *

A. It's very hard to say, if I was taking the notes as someone said it. I don't know if it was my own thinking. But I can tell you today, looking back, it – it – it was a concern and it was a, you know, concern that we had, that the clarity was just not there.

Q. And that clarity raised ethical concerns, correct?

* * *

Q. Or the lack of clarity raised ethical concerns.

* * *

A. Are you saying in my – in my mind or in this –

Q. Well, in your mind, did the lack of clarity raise ethical concerns?

A. It raised concerns to me that, you know, more communications concerns, scientific concerns, medical concerns that – that – that communication was not as clear as it should have been.

Ex. 23 (Gandelman Depo.) at 175:11-176:16.

Defendants' Stock Sales

115. On March 17, 2000, defendant Geis drafted a memo stating that "[n]otification of database closure will be restricted to a limited subset of the Study Team to minimize the potential dissemination of information that might violate SEC regulations regarding disclosure of material information." Ex. 51 at 473.

116. Between August and October of 2000, defendant Geis sold over 75,000 shares of Pharmacia stock at inflated prices for proceeds of approximately $3 million with knowledge of the undisclosed less favorable post-six-month data. Exs. 52-53.

117. Defendant Cox sold approximately $6 million of Pharmacia stock in August and November of 2000. Exs. 54-56.

Other Pharmacia Executive's Stock Sales

118. On May 16, May 18 and November 3, 2000, Pharmacia's Chief Scientific Officer and Chairman of Research and Development Dr. Needleman sold a total of 112,638 shares of Pharmacia stock at inflated prices for proceeds of $5.75 million with knowledge of the undisclosed less favorable post-six-month data. Ex. 98; Ex. 168 (December 8, 2010 Deposition Transcript of Pharmacia Chairman of Research and Development Philip Needleman ("Needleman Depo.") at 119:9-22; Exs. 161, 180.

119. On July 31, 2000, Pharmacia Executive Vice President and Chief of Research and Development Dr. Goran Ando sold 265,958 shares of Pharmacia stock

for proceeds of $13.8 million with knowledge of the undisclosed less favorable post-six-month data. Ex. 40; Ex. 39 (Ando Depo.) at 157:20-158:5; Exs. 161, 180.

120. On May 25, 2000, Pharmacia Senior Executive Vice President and Chief Administrative Officer De Schutter sold 63,830 shares of Pharmacia stock for proceeds of over $3.1 million at inflated prices. Ex. 99.

121. Between July 28, 2000 and August 23, 2000 Pharmacia Chairman of the Board Robert Shapiro sold over 1.7 million shares of Pharmacia stock at inflated prices for proceeds of over $90 million. Ex. 162.

FDA Review of the CLASS Study

122. On or about May 25, 2000, Defendants submitted a supplemental new drug application ("SNDA") to the FDA asking for the removal of the GI warning label from Celebrex, in large part based upon the CLASS study results. Ex. 21 at 112.

123. On September 5, 2000, the FDA announced that it was calling an open meeting of its Arthritis Advisory Committee for February 2001 to consider Defendants' request to remove the GI warning from the Celebrex label. Ex. 61 at 367. An advisory committee is a panel of independent specialists who advise the FDA on issues related to their area of expertise. Ex. 59 (Bowen Report) at 7. The FDA is not required to accept the recommendations of its advisory committees, but it generally does. *Id.*

124. The FDA was not required to hold an advisory committee meeting regarding the Celebrex NDA. *Id.* at 11. Had the FDA elected not to hold such a

meeting, or had the FDA elected to hold a closed meeting, Defendants' submission to the FDA would not normally have become public. *Id.*

125. Defendants held a rehearsal for the advisory committee meeting on January 9, 2001, during which one of the participants commented that "[t]he fact that somebody would have to ask . . . why things went on beyond six months but only a six month analysis is shown indicates shortcomings with the presentation that need to be fixed." Ex. 163 at 540.

126. At another rehearsal on January 17, 2001, Michael Friedman, a Senior Vice President at Pharmacia, stated, "you will be accused of picking an arbitrary time to stop the studies, data dredging, post hoc analyses on risk factors." Ex. 164 at 677.

127. At an advisory committee rehearsal on January 26, 2001, Vibeke Strand, M.D., a paid consultant to Pharmacia, told Defendants, "your presentation . . . was solid, appropriately objective, etc etc, but failed to tell the truth . . . better to present the data as they occurred." Ex. 165 at 632, 634.

128. Prior to the advisory committee meeting, Defendants submitted a briefing document to the FDA summarizing for the committee their request to remove the GI warning label and the CLASS results purportedly supporting that request. Ex. 64. In that briefing document, Defendants argued that the CLASS results after six months had become biased in favor of diclofenac because a disproportionate number of patients taking ibuprofen or diclofenac had withdrawn from the study because they were suffering from symptomatic ulcers or GI symptoms such as abdominal pain. *Id.*

at 42-43. Defendants argued that such patients would have been more likely to later suffer complicated ulcers, such that their withdrawal biased the trial against Celebrex after six months. *Id*. Defendants called this theory "informative censoring," and argued that it rendered the results after the first six months of CLASS confounded or unreliable. *Id*.

129. Defendants' report concluded with regard to CLASS that Celebrex "is associated with a lower rate of ulcer complication relative to conventional NSAIDs." *Id*. at 44.

130. Dr. Lawrence Goldkind, an FDA medical reviewer and gastroenterologist, also prepared a report for the advisory committee. In that report, Dr. Goldkind rejected Defendants' informative censoring argument, stating that Defendants' "***rationale for analyzing the first 6 months as a meaningful endpoint independent of success at the study completion is not convincing***." Ex. 63 at 14. Dr. Goldkind rejected informative censoring in part because, like patients taking diclofenac, patients taking ibuprofen also suffered fewer complicated ulcers as the study went on, but there was no reason to believe that the ibuprofen results were biased. *Id*. at 15. Dr. Goldkind also concluded that even if informative censoring was occurring, "limiting the study to 6 months does not address the statistical concern adequately. . . . One may choose 3, 4 or 5 months to limit the bias." *Id*.

131. Dr. Goldkind also observed that "[o]ne may in fact consider self-selected withdrawal from a drug due to a minor adverse event (before experiencing a more

severe adverse event such as a [complicated ulcer]) to represent a benefit of the drug's overall adverse event profile compared to a drug that is 'silent' in terms of symptoms until a serious adverse event occurs." *Id*. at 14.

132. Dr. Goldkind was not the first person to be skeptical of the informative censoring theory. Two Pfizer Medical Directors, Wahba and Dr. Zwillich, had both openly disagreed with the hypothesis. Ex. 17 (Loose Depo.) at 179:14-18; Ex. 2 (Weiner Depo.) at 121:18-23, 122:5-16; Ex. 166 at 243. Dr. Needleman, the Chairman of Pharmacia's Research and Development, also expressed reservations about the theory. Ex. 167.

133. Having rejected Defendants' informative censoring argument, Dr. Goldkind's report analyzed the results of CLASS from the entire study period and concluded that "[t]he sponsor has failed to demonstrate a statistically significant lower rate of [complicated ulcers] compared to NSAIDs." Ex. 63 at 52.

134. The FDA also asked a statistical reviewer, Hong Laura Lu, Ph.D., to analyze the CLASS data and draft a report for the advisory committee. Ex. 65. Dr. Lu concluded that Defendants' "***rationale for analyzing the first 6 months only . . . is not valid***." *Id*. at 478. Dr. Lu also concluded that the six-month analysis would not be justified even if informative censoring had occurred because patient withdrawals from the study "increased gradually without sudden increase at Month 6." *Id*. at 479. Dr. Lu concluded that Celebrex "did not show significant reduction in [complicated ulcer] incidence compared to two NSAIDs." *Id*.

135. Another FDA reviewer, Dr. James Witter, also prepared a report. Ex. 62. Dr. Witter concluded that the data did "not . . . support the importance of informative censoring in the outcomes." *Id*. at 40.

Disclosure of the Unfavorable CLASS Results

136. On February 6, 2001, the FDA posted Defendants' briefing document to its website along with the briefing documents prepared by Drs. Goldkind, Lu, and Witter. Ex. 66 (October 18, 2010 Affidavit of Howard R. Philips ("Philips Affidavit")), ¶8.

137. Together, the four reports amounted to over 250 pages of statistical analyses and scientific jargon. Exs. 62-65.

138. Scattered throughout these four reports were the five unfavorable CLASS results that Defendants had previously concealed. *Id*.

139. The only public mention of these posting on February 6, 2001, was a *Bloomberg* article entitled "Pharmacia Hasn't Shown Celebrex Safety Benefit, FDA Review Says." Ex. 80 at 1.

140. On February 7, 2001, the advisory committee convened to discuss and recommend to the FDA whether to remove or alter the GI warning on the Celebrex label. Ex. 83.

141. On the morning of February 7, 2001, the FDA reviewers presented the entire study results to the FDA advisory committee. As part of this presentation, Dr. Goldkind stated that "there was no meaningful difference between the three groups"

being compared in the CLASS study and that "no difference was shown between Celebrex and diclofenac." *Id.* at 102-04.

142. Pharmacia also presented the CLASS data to the advisory committee on the morning of February 7, 2001. Ex. 83. However, after Pharmacia had submitted its report to the FDA based upon the first six months of data, the FDA had privately informed Pharmacia that it must present the CLASS results to the advisory committee for the entire duration of the study, not just the first six months. Ex. 59 (Bowen Report) at 23 n.111. Accordingly, Pharmacia's presentation, unlike its report, included CLASS data from the entire study period. Ex. 83 at 56 ("we will focus today's discussion entirely on the entire study results as opposed to the six-month analyses that have been presented in the briefing documents").

143. On February 7, 2001, JP Morgan issued an analyst report discussing the results of the CLASS study. Ex. 86. The analyst report stated that – to analysts' surprise – the FDA's written reviews of the CLASS data are "more negative than expected" and that the "issue of statistical proof of GI superiority vs. NSAIDs [in CLASS] appears thornier than we initially thought." *Id.* at 863. The analyst report also stated:

> The FDA raised four key issues: (1) Pharmacia's choice to analyze the 26 week data exclusively (vs. 52 week data) is incorrect; (2) Celebrex failed to show any statistically significant benefit over one of the comparator NSAIDs (diclofenac); (3) Pharmacia failed to adjust for multiple subgroup analyses, rendering even those P values less than 0.05 in doubt; and (4) ibuprofen plus aspirin was statistically superior to

> either Celebrex or diclofenac plus aspirin (and better than ibuprofen alone).

Id. at 862

144. Dr. Anthony Fiorino, one of the authors of the February 7, 2001 JP Morgan analyst report discussing the CLASS data in detail, testified that "***[o]ur practice was to publish as quickly as possible*** . . . [and] we would do whatever it took to ensure that our reports were out in a timely manner." Ex. 91 (December 7, 2011 Deposition Transcript of Anthony Fiorino, M.D., Ph.D. ("Fiorino Depo.")) at 155:12-156:5.

145. The differences between the six-month and full study period data caused much confusion among the advisory committee members. At the hearing, committee member Dr. Wolfe asked "[h]ow do we have such different presentations this morning? I am really confused. We have, you know, one looks gold and one looks like tin, and I don't understand the differences . . . ." Ex. 83 at 203. Later, committee member Dr. David Wofsy stated, "I shared, and I think many of us did, Dr. Wolfe's concern this morning, the sort of sense that one presentation says white, and the other presentation says black." *Id*. at 212.

146. On the day of the hearing, February 7, 2001, Pharmacia issued a statement representing that CLASS "was an extremely rigorous and complex trial, which made it difficult for the committee to analyze." Ex. 82 at 545. After listening to presentations from Pharmacia, the FDA, and the public on February 7, 2001, the

advisory committee determined, based on the full study data, that Celebrex had neither a GI safety advantage nor a global safety advantage over comparators. Ex. 83 at 160-93.

147. On February 8, 2001, analyst reports were published explaining the disclosures regarding the CLASS trial that occurred over the previous two days. One of the analyst reports was entitled "CLASS Flunks Out," which stated, "FDA Panel Rejects Label Change. An FDA Advisory Committee rejected the notion that Celebrex, a COX-2 inhibitor, has a better safety profile [than] NSAIDs. PHA shares sold off (3+%) based on concerns that Celebrex's growth will stagnate without a label change." Ex. 5 at 589.

148. Between February 6 and February 8, 2001, the closing price of Pharmacia stock dropped $5.28 – over 9%. Ex. 67 (June 7, 2011 Expert Report Concerning Materiality, Loss Causation and Damages by Kenneth M. Lehn ("Lehn Report")), Ex. 4 at 6. Specifically, Pharmacia's closing share price declined over 1% on February 6, 2011, 2.6% on February 7, 2001, and 5.5% on February 8, 2001. *Id*.

149. On February 9, 2001, Pharmacia prepared a document entitled "Q&A: FDA Advisory Committee Hearing on Proposed GI Safety Label Revision for Celebrex." That document stated in part, "[d]ue to the complexity of the CLASS data, the advisory panel on day one (February 7) experienced difficulty interpreting the results. After reviewing data from VIGOR study [about VIOXX] on February 8, the Committee subsequently provided guidance that the labels for both CELEBREX and

VIOXX should reflect data showing gastrointestinal safety advantages versus specific comparator NSAIDs studied." Ex. 168 at 326.

Economic Analysis of the Decline in Pharmacia's Stock Price

150. Plaintiffs' economic expert witness, Stephen Feinstein, Ph.D., performed an event study to test the efficiency of the market for Pharmacia's stock during the relevant time period to investigate the responsiveness of Pharmacia's stock price to information about the company and Celebrex and to identify any abnormal declines in Pharmacia's stock price in response to information about the company or the CLASS study. Ex. 6 (Feinstein Report) at 27-54; Ex. 81 (October 19, 2011 Deposition Transcript of Steven Feinstein, Ph.D. ("Feinstein Depo.")) at 11:19-25.

151. The price decline between February 6 and 8, 2001 was statistically significant, as were the declines on February 7 and February 8, 2001 individually. Ex. 3 (October 28, 2011 Deposition Transcript of Defendants' Causation Expert Kenneth Lehn ("Lehn Depo.")) at 17:11-16; Ex. 6 (Feinstein Report) at 70 & Ex. 12

152. The decline in Pharmacia's stock price between February 6 and February 8, 2001 cannot be explained by general economic conditions, stock-market-wide factors, or macro-economic factors. Ex. 6 (Feinstein Report) 68-74; Ex. 81 (Feinstein Depo.) at 68:7-74:8; Ex. 3 (Lehn Depo.) at 18:22-19:12.

153. The decline in Pharmacia's stock price between February 6 and February 8, 2001 cannot be explained by industry-specific factors. Ex. 6 (Feinstein Report), Ex.

12; Ex. 81 (Feinstein Depo.) at 68:7-74:8; Ex. 3 (Lehn Depo.) at 18:22-19:12, 268:13-24.

154. The decline in Pharmacia's stock price between February 6 and February 8, 2001 cannot be explained by the disclosure of any other Pharmacia-specific information other than the previously undisclosed, adverse results from the CLASS study. Ex. 6 (Feinstein Report) at 54-74.

155. Defendants' economic expert witness, Dr. Kenneth Lehn, has not offered an opinion on what caused Pharmacia's stock to decline on February 8, 2001. Ex. 3 (Lehn Depo.) at 102:6-16, 117:7-22, 221:19-25, 238:2-8.

Pharmacia's February 12, 2001 Conference Call

156. On February 12, 2001, Pharmacia held a conference call with investment analysts. Ex. 169.

157. On that call, defendant Cox stated, "[i]n terms of the situation for Celebrex moving forward, the *JAMA* paper, as I mentioned, was published in September, and that contains the results from the long-term outcomes studies. I think we've had a lot of benefit in the marketplace of being able to use the data." *Id.* at 430-31.

Internal Company Communications in 2001 and 2002

158. On May 25, 2001, Pharmacia scientist Dr. Kenneth Verburg sent an email to defendant Geis stating "[c]ombined endpoint is post-hoc and assigning p-

values is not defensible. . . . Non-ASA patient data is data-dredging to find positive data." Ex. 75.

159. On March 1, 2001 Ethan Weiner, M.D. a Pfizer Vice President wrote to Lori Shafner ("Shafner") a Pfizer employee in an email that "I am strongly opposed to say we beat the aggregated NSAIDs as well as ibu individually. It's ***misleading***." Ex. 71 at 999.

160. On August 19, 2001, Pfizer employee Shafner wrote an email to several colleagues that referenced the transcripts of the advisory committee hearings on February 7 and 8, 2001. Specifically, Shafner writes that the transcripts "take days to review." Ex. 170 at 026.

161. On August 28, 2001, Dr. Weiner wrote in an internal Pfizer email that "[h]aving shown with CLASS that six month results can look different from one year results, will anything less than a year (especially three months) ever be taken seriously? I doubt it." Ex. 171 at 679.

162. On January 28, 2002 Pfizer employee Leland Loose wrote an email to colleagues in which he stated that "CLASS had about 8,000 patients and ran for about a year with a cut of data at 6 months . . . . If you look at labels these big ticket studies got a big goose egg so I don't see their value yet." Ex. 172 at 316.

The Aftermath

163. On August 5, 2001, *The Washington Post* published an article by Susan Okie entitled "Missing Data on Celebrex; Full Study Altered Picture of Drug," which stated in relevant part:

> When editors of the Journal of the American Medical Association sent medical expert M. Michael Wolfe an unpublished study on the blockbuster arthritis drug Celebrex last summer, he was impressed by what he read.
>
> Tested for six months in a company-sponsored study involving more than 8,000 patients, the drug was associated with lower rates of stomach and intestinal ulcers and their complications than two older arthritis medicines – diclofenac and ibuprofen.
>
> JAMA's editors wanted to rush the findings into print, and Wolfe and a colleague provided a cautiously favorable editorial to accompany it. But in February, when Wolfe was shown the complete data from the same study as a member of the Food and Drug Administration's arthritis advisory committee, he said he saw a different picture.
>
> "We were flabbergasted," he said.
>
> The study – already completed at the time he wrote the editorial – had lasted a year, not six months as he had thought, Wolfe learned. Almost all of the ulcer complications that occurred during the second half of the study were in Celebrex users. When all of the data were considered, most of Celebrex's apparent safety advantage disappeared.
>
> "***I am furious. . . . I wrote the editorial. I looked like a fool***," said Wolfe, a Boston University gastroenterologist. "But . . . all I had available to me was the data presented in the article."
>
> JAMA's editor, Catherine D. DeAngelis, said the journal's editors were not informed about the missing data. "***I am disheartened to hear that they had those data at the time that they submitted [the manuscript] to us," she said. "We are functioning on a level of trust that was, perhaps, broken***."

* * *

> After reviewing the full study, the FDA's arthritis advisory committee concluded that Celebrex offers no proven safety advantage over the two older drugs in reducing the risk of ulcer complications, said FDA spokesman Susan Cruzan. The company has requested a change in the drug's labeling to state that it is indeed safer, but the FDA has asked for additional information before making a decision.
>
> Meanwhile, the JAMA article and editorial have likely contributed to Celebrex's huge sales. "When the JAMA article comes out and confirms the hype, that probably has more impact than our labeling does," said Robert J. Temple, director of medical policy at the FDA's Center for Drug Evaluation and Research.

Ex. 68.

164. On August 12, 2001, the London *Sunday Times* published a story entitled "Move to open all drug test results," which stated in relevant part:

> THE world's most prominent medical journals, including The Lancet and the British Medical Journal, have joined forces to stop drug firms "cheating" on medical studies and refusing to publish bad results.
>
> The move follows a case where Pharmacia, which owns Monsanto, the GM seed firm, last year was accused of duping the Journal of the American Medical Association (JAMA) into publishing favourable results from a study of the arthritis drug Celebrex.
>
> The six-month study on 8,000 patients claimed Celebrex was associated with lower rates of stomach and intestinal ulcers than two other older arthritis medicines. In fact, the study took a year and the final results showed that almost all of the ulcer complications occurring in the second, unpublished half, were in Celebrex users.
>
> Medical editors around the world will now refuse from next month to print drug-company sponsored studies unless the researchers involved are guaranteed scientific independence. One described the action as an attempt to "give scientists clout with drug companies."

> Dr. Michael Wolfe, an American expert in the field, who had given the study a favourable review in the JAMA, said: "***I thought I was looking at a completely different study. The politically correct term is data discrepancy – but I call it scientific fraud. I believe Pharmacia cheated***."

Ex. 173.

165. The November 11, 2001 edition of JAMA contained several letters to the editor concerning the September 13, 2000 CLASS article. Ex. 31. The first letter, by Jennifer Berg Hrachovec, Pharm.D., M.P.H., and Marc Mora, M.D. of the Pharmacy and Therapeutics Committee Group Health Cooperative in Seattle, Washington, stated:

> The authors of the CLASS trial reported that celecoxib [Celebrex] caused fewer symptomatic ulcers and ulcer complications than did diclofenac or ibuprofen at 6 months of follow-up. ***We are concerned that subsequent information from the trial, which is available on the US Food and Drug Administration (FDA) Web site, appears to contradict these conclusions***. As described on the FDA Website, the published CLASS trial differs from the original protocol in primary outcomes, statistical analysis, trial duration, and conclusions. In particular, the unpublished data show that by week 65, celecoxib [Celebrex] was associated with a similar number of ulcer complications as diclofenac and ibuprofen.
>
> * * *
>
> We believe that the complete findings of the CLASS trial should be made widely known.

Id. at 2398

166. The next letter to the editor was written by James Wright, M.D., Ph.D., Thomas L. Perry, M.D., Ken L. Bassett, M.D., and G. Keith Chambers, M.D., from the University of British Columbia, Vancouver, which stated in relevant part:

> The FDA found that "For upper GI safety, and also for global safety, there does not appear to be any meaningful advantage for Celebrex."
>
> However, the published report of the CLASS trials draws the opposite conclusion. This is because the published article represents selective reporting of the combined analysis of only the first 6 months of 2 separate protocols of longer duration . . . .
>
> * * *
>
> ***The unfortunate result of the selective and partial reporting of the CLASS study is that it could mislead physicians and patients.***

Id. at 2398-99.

167. In response to these letters, three of the Pharmacia-paid authors of the JAMA article, Drs. Silverstein and Simon, and Gerald Faich, M.D. published their own letter in the same issue of JAMA, which stated:

> ***In retrospect, we acknowledge that we could have avoided confusion by explaining to the JAMA editors why we chose to inform them only of the 6-month analyses and not the longer-term data that were available to us when we submitted the manuscript***.

Id. at 2399.

168. On December 7, 2001, the advisory committee held a closed meeting to update its members on the safety of Cox-2 inhibitors which included a presentation of Celebrex data. Ex. 59 (Bowen Report) at 14 n.38. Because it was a closed meeting, no reports were posted to the public. *Id.* at 14.

169. On June 1, 2002, BMJ published an editorial by Dr. Juni, et al. about the JAMA article that stated in relevant part:

> [The CLASS study] authors' explanations for these serious irregularities [in the CLASS study] were inadequate. They failed to justify the post hoc changes in design, outcomes, and analysis and provided an unconvincing explanation for considering the six month follow up only.
>
> * * *
>
> ***Publishing and distributing overoptimistic short term data using post hoc changes to the protocol, while omitting disappointing long term data of two trials, which involved large numbers of volunteers, is misleading.***

Ex. 69 at 312-13.

170. On June 6, 2002, the FDA approved a new label for Celebrex. The label included the exact same GI warning it contained before the CLASS study was conducted. Ex. 59 (Bowen Report) at 26 n.132. The new label included some data regarding ulcer rates from the CLASS study, but no ulcer rate comparisons to ibuprofen, diclofenac, or any other NSAID. Ex. 174.

171. On June 24, 2002, *Business Week* ran an article in which JAMA deputy editor Drummond Rennie stated that the study's authors, including Pharmacia, "'were not open with us . . . [t]hey signed letters saying the studies have all the relevant stuff,' but 'they had contradictory results when they sent us this paper, and they should have revealed them to us. And they didn't.'" Ex. 175.

172. Pharmacia merged with Pfizer in a stock for stock exchange on April 16, 2003.

173. In December of 2003, an article based upon the full CLASS data was submitted to JAMA. Ex. 176. Finally able to review the complete CLASS data, JAMA refused to publish the article. Ex. 49 (Simon Depo.) at 176:2-177:1. Subsequently, JAMA altered its conflicts of interest policy in part because of the JAMA article about CLASS. Ex. 177; Ex. 9 (De Angelis Depo.) at 103:19-23.

174. In March 2005, the FDA was preparing for another advisory committee meeting regarding Celebrex. In preparation for that meeting, Dr. Witter, an FDA medical reviewer, wrote in an email, "***the comparisons in the JAMA paper [regarding CLASS] are misleading in that they do not include the entire study results which would have shown that the difference noted at 6 months in non-aspirin users was not sustained to the end of the study***." Ex. 66 (Philips Affidavit), Attachment D.

175. On April 7, 2005, the FDA required that the Celebrex label include a "black box" warning regarding GI side-effects. Ex. 178. A black box warning is the strongest warning the FDA can use on a drug label. Ex. 107 (Bowen Depo.) at 352:16-353:15.

176. On December 16, 2005, National Public Radio broadcast an interview with Catherine De Angelis, M.D., the Editor in Chief of JAMA. Ex. 179. Regarding the authors of the JAMA article, Dr. De Angelis stated "***[t]hey deliberately lied***. . . . When they went out to 12 months, it turned out there was not difference. And then we

got into trouble and we made them write a letter describing what they had done and admitting that they had lied to us." *Id.*

DATED: March 2, 2012

COHN LIFLAND PEARLMAN
HERRMANN & KNOPF LLP
PETER S. PEARLMAN

s/ Peter S. Pearlman
PETER S. PEARLMAN

Park 80 West – Plaza One
250 Pehle Avenue, Suite 401
Saddle Brook, NJ 07663
Telephone: 201/845-9600
201/845-9423 (fax)

Liaison Counsel

ROBBINS GELLER RUDMAN
& DOWD LLP
PATRICK J. COUGHLIN
ARTHUR C. LEAHY
SCOTT H. SAHAM
LUCAS F. OLTS
MATTHEW I. ALPERT
JENNIFER L. GMITRO
655 West Broadway, Suite 1900
San Diego, CA 92101
Telephone: 619/231-1058
619/231-7423 (fax)

SCOTT + SCOTT LLP
CHRISTOPHER M. BURKE
MATTHEW P. MONTGOMERY
DAVID H. GOLDBERGER
707 Broadway, 10th Floor
San Diego, CA 92101
Telephone: 619/233-4565
619/233-0508 (fax)

MOTLEY RICE LLC
JOSEPH F. RICE
LANCE OLIVER
JOSHUA C. LITTLEJOHN
28 Bridgeside Blvd.
Mount Pleasant, SC 29464
Telephone: 843/216-9000
843/216-9450 (fax)

Counsel for Plaintiffs

SUGARMAN & SUSSKIND
ROBERT SUGARMAN
2801 Ponce De Leon Blvd., Suite 750
Coral Gables, FL 33314
Telephone: 305/529-2801
305/447-8115 (fax)

Additional Counsel for Plaintiffs